

REMARKS

By way of the foregoing amendment, Claims 1-11, 14-27, and 30-33 are pending. Claims 4, 5, 12, and 13 were previously withdrawn without prejudice or disclaimer in Applicants' Response dated November 5, 2007. Claims 12-13 and 28-29 are hereby canceled without prejudice or disclaimer to the subject matter therein. Claims 1, 14 and 24 have been amended without prejudice or disclaimer. Claims 31-33 have been newly added. Support for the foregoing amendment can be found throughout the specification and claims as originally filed, for example, at page 31, lines 4 to 25; page 37, line 27 to page 38, line 7; and Table 1. No new matter enters by way of the foregoing amendment.

I. Election/Restrictions

Applicants thank the Examiner for acknowledging Applicants' election without traverse of Group XV, claims 1-3, 6-11, and 14-29 to the extent the claims are drawn to SEQ ID NO: 2. Applicants understand that if claim 1 is found allowable, Applicants retain the right to rejoin the non-elected claims of Groups I and VIII in the instant application.

II. Rejection under 35 U.S.C. § 112, Second Paragraph, Indefiniteness

Claim 27 stands rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. *Office Action* at page 2. The Examiner alleges that claim 27 is indefinite in the recitation of "at least partially reducing the level of a transcript", given that it is unclear how this differs from "reducing the level of a transcript", and therefore the metes and bounds of the claims remains unclear. *Id.* Applicants respectfully disagree and specifically draw the Examiner's attention to the fact that the phrase "at least partially reducing the level of a transcript" is defined in the specification. For example, the specification provides that "'a partial reduction' of the level of an agent such as a protein, fatty acid, or mRNA means that the level is reduced at least 25% relative to a cell or organism lacking a nucleic acid molecule capable of reducing the agent." *See* Specification at page 12, lines 31-33. Applicants therefore respectfully request reconsideration and withdrawal of the indefiniteness rejection of claims 27 under 35 U.S.C. § 112, second paragraph.

III. Rejection under 35 U.S.C. § 112, First Paragraph, Enablement

Claims 14-29 stand rejected under 35 USC § 112, first paragraph, because allegedly, the claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. *Office Action* at page 3. This rejection is respectfully traversed for at least the reasons which follow.

The Examiner alleges that “the specification does not disclose any soybean seeds transformed with (the claimed) constructs and the specification does not disclose any soybean plants having reduced levels of either palmitic or stearic acid relative to a nontransformed plant.” *Office Action* at page 3. Applicants respectfully disagree with the Examiner’s assertion. Applicants have provided considerable direction and guidance, and have presented working examples such that it is well within the level of ordinary skill in the art to make and/or use the invention. The specification provides working examples of soybean plants transformed with a recombinant nucleic acid molecule comprising as operably linked components: a promoter that functions in a plant cell to cause production of an mRNA molecule; a soybean *FATB* intron sequence, and a delta-9 desaturase gene. Moreover, the specification teaches that soybean plants transformed with the described recombinant nucleic acid molecule demonstrate an alteration in saturated fatty acids levels as compared to those of the seed from non-transformed soybean plants, namely a reduction in saturated fatty acid levels (palmitic and stearic acid). *See, e.g.*, Specification at page 36, lines 31 to page 40, line 2 (Examples 2 and 3, Table 1).

The specification also provides significant additional guidance for a skilled artisan to make and/or use the invention. For instance, the specification provides significant guidance regarding the cloning and preparation of constructs for the expression of intron sequences from soybean *FATB* genes, including soybean *FATB* intron I, as well as a beta-ketoacyl-ACP synthase I, beta- ketoacyl-ACP synthase IV, or delta-9 desaturase encoding sequences. *See, e.g.*, Specification at page 23, line 12 to page 25, line 3 and at page 35, line 15 to page 36, line 19. Moreover, the specification teaches various methods for the introduction of the expression

constructs into plant cells. *See, e.g.*, Specification at page 27, lines 10 to 27. Furthermore, not only does the specification teach the sense and antisense expression of a soybean *FATB* intron in a plant for the modification of fatty acid saturation (*See, e.g.* Specification at page 28, line 3 to page 29, line 4), the specification also teaches modifications of fatty acid compositions (*See, e.g.*, Specification at page 31, line 4 through page 32, line 7). From such disclosure, it is well within the level of ordinary skill in the art to design expression constructs to reduce saturated fatty acid levels in a soybean plant without the need for undue experimentation within the claims as currently amended.

The Examiner alleges that the claims either provide no limitation with regard to an altered phenotype of the transgenic plant or several different phenotypes for the claimed soybean plants and seeds. *Office Action* at page 5. Applicants respectfully disagree with the Examiner's statement. Applicants respectfully assert that the specification teaches that intron sequences of a *FATB* gene, when introduced into a soybean plant, are capable of selectively reducing the level of an endogenous *FATB* protein and/or endogenous *FATB* transcript, thereby resulting in a modification of the fatty acid biosynthetic pathway and a consequent decrease in the levels of saturated fatty acids in soybean plant. *See* Specification at page 11, line 30 to 12, line 3. Furthermore, the specification teaches that non-coding sequences of a *FATB* gene may also be used in combination with nucleic acid sequences coding for enzymes such as beta-ketoacyl-ACP synthase I, beta- ketoacyl-ACP synthase IV, and delta-9 desaturase, which further modifies the fatty acid biosynthetic pathway and further decreases the level of saturated fatty acids in the cell or organism. *See* Specification at page 12, lines 2 to 6. Additionally, the specification teaches that plant seeds comprising a decreased amount of *FATB* exhibit a decreased percentage of saturated fatty acids, such as palmitate and stearate. *See* Specification at page 26, lines 1-3. One of skill in the art having read the specification would appreciate that DNA sequences capable of suppressing *FATB* and expressing a beta-ketoacyl-ACP synthase I, beta- ketoacyl-ACP synthase IV, or delta-9 desaturase, respectively, would decrease the percentage of saturated fatty acids, such as palmitate and stearate when expressed in plant seeds. *Id.* at page 36, lines 31 to page 40, line 2.

The Examiner has not met the evidentiary burden to impose an enablement rejection. A specification that discloses how to use a claimed invention "must be taken as in compliance with

the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein.” *In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995), *quoting In re Marzocchi*, 439 F.2d 220, 223, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971) (emphasis in original). Applicants have provided considerable direction and guidance, and have presented working examples such that it is well within the level of ordinary skill in the art to practice the invention without undue experimentation. The Examiner has not provided sufficient evidence to cast doubt on the guidance provided in the specification. Rather, the Examiner has provided generalizations regarding a lack of predictability in the art and the need for some experimentation.

The Examiner cites to De Luca *et al.* (*AgBiotech News and Information* Vol. 5 No. 6 :255N-229N, 1993) (“De Luca”) to support the general proposition that “modifying plant biosynthetic pathways by transforming plants with genes encoding enzymes involved in said pathway is highly unpredictable.” *Office Action* at page 3. At the outset, Applicants respectfully submit that “general unpredictability” is not enough to render the claimed invention unachievable to one skilled in the art. To the extent that the Examiner suggests there is a requirement for *a priori* predictability without recourse to any experimentation, that position is without legal support. *Cf. Atlas Powder Co. v. E. I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1576, 224 U.S.P.Q. 409, 413 (Fed. Cir. 1984) (“[t]hat some experimentation is necessary does not preclude enablement”). The proper test of enablement in such a situation is whether the disclosure “adequately guide[s] the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility.” *See In re Vaeck*, 947 F.2d 488, 496, 20 U.S.P.Q.2d 1438, 1445 (Fed. Cir. 1991). It is well within the level of skill in the art to prepare expression constructs, transform plants and analyze the fatty acid saturation without undue experimentation based on the extensive guidance disclosed in the present specification. Further, it is submitted that the specification discloses sufficient guidance to render the results predictable within the context of the transformed plants and methods of the invention. In fact, by providing guidance as to the selection of nucleic acid sequences (*See, e.g.*, Specification at page 15, lines 6 to page 16, line 30), various soybean *FATB* intron sequences (*See, e.g.*, Specification at page 19, line 13 to 25), the design and preparation of expression constructs (*See, e.g.*, Specification at page 23, line 12 to page 25, line 3 and at page 35, line 15 to

page 36, line 19), and the demonstration of the modification of fatty acid saturation consistent with such guidance (*See, e.g.*, Specification at page 31, line 4 through page 32, line 7), Applicants have demonstrated that the present disclosure enables the claimed transformed plants and methods.

De Luca ascribes the alleged unpredictability to “our poor understanding of plant metabolic pathways and their *in vivo* regulation” (see the paragraph bridging the columns on page 225N). The Office does not suggest that there is a poor understanding of fatty acid biosynthesis or its *in vivo* regulation. Instead, De Luca reports of “spectacular results” (see the last paragraph on page 228N) and cites a successful example of altering plant fatty acid biosynthesis (see first full paragraph of 228N). Moreover, De Luca, published in 1993, is not an appropriate reference to determine the state of the art when the instant application was first filed in March 21, 2002. Given this, one of skill in the art at the time the invention was made would not question the enablement of the claimed invention on the basis of De Luca.

The Examiner also cites to Voelker *et al.* (*Annual Review of Plant Physiology and Plant Molecular Biology*, 52: 335-361, 2001) (“Voelker”) to set forth the “complexity of plant lipid biosynthesis and the uncertainty of the resultant seed fatty acid composition when transforming plant species with heterologous genes.” *Office Action* at page 3. In supporting the rejection, the Examiner alleges that Voelker teaches that “plants transformed with fatty acid biosynthesis genes from heterologous plant species do not always have fatty acid profiles that correspond to those of the plant from which the gene was cloned.” *Id.* at page 5 (citations removed). Moreover, the Examiner uses the teachings of Voelker to assert that “transformation of a plant with a FATB thioesterase coding sequence resulted in increased levels of the saturated fatty acid, laurate, as opposed to a decrease in saturated fatty acids, which is claimed.” *Id.* Even assuming, *arguendo*, that these statements are true, the Examiner has misapplied Voelker’s alleged teaching of “unpredictability” to the present invention.

Contrary to the Examiner’s assertions, the claimed invention has nothing to do with transforming plant species with heterologous genes. Rather, soybean seeds of the claimed invention include a genome with a nucleic acid sequence that suppresses the expression of endogenous soybean *FATB* in soybean, not genes from heterologous plant species. Moreover,

Applicants are not claiming the method by which the invention was created; rather, the claims are directed to compositions. Here, Applicants are claiming compositions, namely, soybean plants transformed with a nucleic acid molecule including a soybean *FATB* intron, and such plants were achieved by the Applicants. The working example provided in the specification demonstrates with *certainty*, and not unpredictability, that the use of soybean *FATB* introns for the suppression of endogenous soybean *FATB* in soybean plants resulted in a decrease in saturated fatty acid levels.

The Examiner also cites Topfer *et al.* (*Science* 268: 681-685) apparently as support that overexpression of a *Cuphea* *FATB* thioesterase results in an unpredictable fatty acid expression levels. *Office Action* at page 6. As such, Topfer *et al.* also appears inapplicable to the claimed invention as the present invention employs the use of soybean *FATB* introns for the suppression of endogenous soybean *FATB*. The *FATB* intron recited in the claims is not expressing a functional protein as in Topfer *et al.*. In response to the alleged unpredictability of plant fatty acid phenotypes set forth by Voelker and Topfer *et al.*, Applicants respectfully assert that the enablement requirement is satisfied as long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim. MPEP § 2164.01(b). Applicants have satisfied this requirement by providing a working example of soybean seeds exhibiting a reduced saturated fatty acid content. *See* Specification at page 36, lines 31 to page 40, line 2 (Examples 2 and 3, Table 1). The Examiner has not provided sufficient applicable evidence to discredit the teaching in the specification.

The Examiner further alleges that the specification does not provide guidance with regard to selecting for transformed plants and seeds from the plants produced by the transformation with any of the vast multitude of possible constructs that are claimed. *Office Action* at page 6. As previously discussed, the specification provides ample guidance to the skilled artisan as to the choice of nucleic acid sequences. Furthermore, the specification recites well-known methods to select for transformed plants, such as gas chromatography. *See* Specification at page 37, line 33. Even assuming, *arguendo*, that the Examiner's generalization regarding the unpredictable state of the art is accepted, the conclusion that undue experimentation would be required to practice the claimed method is inconsistent with the current state of the law. Specifically, the law provides that experimentation is not necessarily undue simply because it is complex, if the art

typically engages in such experimentation. *See In re Certain Limited-Charge Cell Culture Microcarriers*, 221 U.S.P.Q. 1165, 1174, (Int'l Trade Comm'n 1983) *aff'd. sub nom.*, *Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, 227 U.S.P.Q. 428 (Fed. Cir. 1985). Moreover, performing routine and well-known steps, such as evaluating transformed plants, and fatty acid analysis, cannot create undue experimentation even if it is laborious. *See In re Angstadt*, 537 F.2d 498, 504, 190 U.S.P.Q. 214, 218-219 (C.C.P.A. 1976).

Applicants have provided considerable direction and guidance, and have presented a working example such that it is within the level of ordinary skill in the art to practice the invention without undue experimentation. In contrast, the Examiner has not provided specific or sufficient evidence to cast doubt on the guidance provided in the specification. Rather, the Examiner has provided generalizations regarding a lack of predictability in heterologous protein expression in plants and the need for some experimentation.

Accordingly, for at least these reasons, it is submitted that the claims are sufficiently enabled under 35 U.S.C. § 112, first paragraph, and withdrawal of this rejection is respectfully requested.

IV. Rejection under 35 U.S.C. § 103

Claims 1, 2, 7, 8, 10, and 11 stand rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Dehesh *et al.* (*Plant J*, 15(3) 383-390, 1998) taken with Shoemaker *et al.* (Database Accession AW568268, 3 Dec 2001). *Office Action* at page 7. Applicants disagree.

The Examiner alleges that, “[g]iven the recognition of those of ordinary skill in the art of having the construct of Dehesh *et al.* comprising a plant seed-specific promoter operably linked to a plant *FATB* sequence and optionally to a second fatty acid biosynthesis gene, such as KAS IV for modulating fatty acid levels when transformed into a plant, it would have been obvious to modify this construct by substituting other known thioesterase coding sequences, such as that of SEQ ID NO: 2, as taught by Shoemaker *et al.*” *Office Action* at page 8. Applicants respectfully disagree with the Examiner. At the outset, Shoemaker *et al.* does not teach SEQ ID NO: 2 as alleged by the Examiner. *Id.* There are 40 nucleotides missing from Shoemaker *et al.* as compared to SEQ ID NO: 2.

Moreover, to establish a *prima facie* case of obviousness, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of skill in the art, to modify the reference or to combine reference teachings. The teaching or suggestion to make the claimed combination must be found in the prior art, and not based on the applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Applicants respectfully assert that the Examiner has failed to establish a *prima facie* case of obviousness because the Examiner has not provided an adequate explanation of the suggestion or motivation to combine the teachings of Dehesh *et al.* with Shoemaker *et al.* The Examiner alleges that "Dehesh et al teach a recombinant nucleic acid comprising a napin seed-specific promoter operably linked to a FATB thioesterase gene sequence and said construct further comprising a coding sequence for a KAS IV gene." *Office Action* at page 7 (citation omitted). First, Applicants understand Dehesh *et al.* to have generated plants co-expressing KAS IV with different thioesterases by crossing lines overexpressing the two different genes and not by expression of one construct with both genes as alleged by the Examiner. *See Dehesh et al.* at page 389, 1st column at bottom. Second, even if the construct of Dehesh et al. has both genes as alleged, the Examiner appears to be alleging, without pointing to evidence, that one of ordinary skill in the art would have the motivation to replace a functional FATB thioesterase with the nucleotides of Shoemaker *et al.*. A bold assertion is not enough to prove the basis for a motivation to combine and Applicants respectfully request that the rejection be withdrawn.

"The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990)." MPEP § 2143.01. In rejecting claims 3, 6, and 9, the Examiner appears to believe that the motivation to combine Dehesh *et al.* with Shoemaker *et al.* is to modulate fatty acid levels in a plant. *Office Action* at page 9. The Examiner has failed to establish that there would have been motivation to modify the alleged combined KASIV/FATB construct of Dehesh *et al.* by replacing a full-length FATB thioesterase gene, capable of overexpressing the thioesterase in a plant, with the 64 nucleotide EST sequence recited in Shoemaker *et al.* to modulate fatty acid levels in a plant.

"Rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning **with some rational underpinning** to support

the legal conclusion of obviousness.” *KSR Int’l. Co. v. Teleflex, Inc.*, 127 S.Ct. 1727,1741 (2007) quoting *In re Kahn* 441 F.3d 977, 988 (Fed. Cir. 2006) (emphasis added). Applicants therefore respectfully disagree with the Examiner’s assertion that one of skill in the art would have been motivated to combine the teachings of Dehesh *et al.* with Shoemaker *et al.* Further to the arguments provided above, Applicants have amended claim 1 to facilitate prosecution, and respectfully assert that the rejection of claims 1, 2, 7, 8, 10, and 11 under 35 U.S.C. § 103 is now moot.

Claims 3, 6, and 9 are further rejected under 35 USC § 103(a) as being allegedly unpatentable over Dehesh *et al.* taken with Shoemaker *et al.* as applied to claims 1, 2, 7, 8, 10, and 11 above, further in view of Applicants’ admitted state of the prior art. *Id.* Applicants respectfully traverse this rejection. Applicants acknowledge that the Specification teaches that delta-9 desaturases, 7S seed specific promoters, and the use of double-stranded RNA for gene suppression were known in the prior art. However, Applicants respectfully disagree with the Examiner’s assertion that, given these admissions by the Applicants, the claimed invention would have been *prima facie* obvious as a whole at the time it was made. Applicants respectfully submit that the rejection of dependent claims 3, 6 and 9 has been overcome by the arguments set forth above with respect to the rejection of claim 1 under 35 U.S.C. § 103. Applicants respectfully request reconsideration and withdrawal of these rejections.

CONCLUSION

In view of the above, each of the presently pending claims is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejections of the claims, and to pass this application to issue. The Examiner is encouraged to contact the undersigned at (202) 942-5186 should any additional information be necessary for allowance.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Kristan Lansbery", with a long horizontal flourish extending to the right.

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Date: April 29, 2008

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